# AATB Annual Meeting
# Sept. 9-12, 2006
# San Diego

## FDA Update

**Ruth Solomon, M.D.**

**Director, DHT**

**OCTGT, CBER, FDA**

# FDA Update

- **Division of Human Tissues**
- **Registration**
- **Donor Eligibility**
- **CGTPs**
- **Exemptions and Alternatives**
- **Adverse Reactions**
- **HCT/P Deviations**
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# Division of Human Tissue

- **DHT Director**--Ruth Solomon, M.D.
- **Human Tissue and Reproductive Branch Chief**--Martha Wells, M.P.H., RAC
- **Staff**
  - Melissa Greenwald, M.D.
  - Ellen Lazarus, M.D.
  - Laura St. Martin, M.D., M.P.H.
  - Jackie Neidinger, B.A., CTBT
  - Rose Wiseman
- **Staff Wannabee's**
  - Trey Jamison Greenwald
  - Dessa Elizabeth Neidinger

# Registration

- **Total (as of 8/06) = 2322**
  - **Musculoskeletal = 1160**
  - **Hematopoietic stem cell = 613**
  - **Repro = 606**

- **www.fda.gov/cber/tiss.htm**
- **tissuereg@cber.fda.gov**

# Registration cont.

- **Failure to Register**
  - **If you do not register or renew your registration annually, you will receive a letter telling you to do so in April.**
  - **If you still do not register, we will e-mail the responsible person listed in the registration database; OCBQ will contact district offices**
  - **A Failure to Register Notice has been posted on CBER's website**
    - **www.fda.gov/cber/tissue/failreg.htm**

# Registration, cont.

- **Annual update of registration required annually, in December**
- **Changes to Listing are required within 6 months**
- **Change of ownership or location required within 5 days**
- **Inactivation—check box #2(d)**
- **Electronic registration is encouraged**

# Donor Eligibility

- **Final Guidance will publish soon**
- **Donor Screening Tests for Testing HCT/P Donors**
- **www.fda.gov/cber/tissue/prod.htm**
  - **Licensed Donor Screening Tests—includes sample type; whether licensed for cadaveric**
  - **Cleared NAT for Chlamydia trachomatis and Neisseria gonorrhea**

# CGTPs

- Draft guidance in progress
- Input from AATB, EBAA, and others
- CGTP Rule—reminder
  - 1271.150(c)(1) Manufacturing Arrangement
    - (iii) Before entering into a contract, agreement, or other arrangement with another establishment to perform a step in manufacture for you, you must ensure that the establishment complies with applicable CGTP requirements (CGTP includes DE)

# CGTPs, continued

- **If during the course of this contract, agreement, or other arrangement, you become aware of information suggesting that the establishment may no longer be in compliance with such requirements, you must take reasonable steps to ensure that the establishment complies with those requirements.**
- **If you determine that the establishment is not in compliance with those requirements, you must terminate your contract, agreement, or other arrangement with the establishment.**
- **(See CGTP preamble—comments 28-30)**

# Exemptions and Alternatives

- **OCTGT SOPP 9151 6/13/06**
  - **DHT coordinates**
  - **Database**
  - **Consults others outside of division**
  - **Draft letter presented to Tissue Policy Team**
  - **Center Director sign-off**

# Adverse Reactions

- **Guidance for Industry:**
- **MedWatch Form FDA 3500A: Mandatory Reporting of Adverse Reactions Related to HCT/Ps**

- **www.fda.gov/cber/gdlns/advhctp.htm**

# Adverse Reaction Reports--Internal Procedures

- SOPP 8508 describes procedures for handling AR reports—coordination by 5 offices in CBER
- www.fda.gov/cber/regsopp/8508.htm
- MedWatch reports involving HCT/Ps come to CBER
- Entered into 2 databases: AERS and AEPP
- Follow-up infectious adverse reactions
- All information and follow-up information are entered into AEPP database
- Review by OCTGT, OBE, OCBQ
- Seek more information from reporter and manufacturer
- Develop categories for classifying “conclusions”

# Adverse Reaction Reports Statistics—Nov. ’05 to July ‘06

- **Total = 152**
- **Product Type**
  - **Tissues—108 (71%)**
  - **Cells---------44 (29%)**
- **Tissue Type**
  - **Bone—39 (36%)**
  - **Eye ----26 (24%)**
  - **Skin----23 (21%)**
  - **Soft Tissue—9 (8%)**
  - **Cardiac—8 (7%)**
- **Reports from**
  - **Manufacturers---------54%**
  - **Healthcare workers—46%**
- **Infectious/Non-infectious----80%/20%**

# HCT/P Deviation
# 21 CFR 1271.3(dd)

- An event that represents a deviation from applicable regulations, standards or established specifications that relate to prevention of communicable disease transmission or contamination, or
- An unexpected or unforeseeable event that may be related to transmission or potential transmission of a communicable disease or may lead to HCT/P contamination

# HCT/P Deviation Reporting 21 CFR 1271.350(b)

- Required for “361” nonreproductive HCT/Ps recovered on or after 5/25/05
- Related to a distributed HCT/P
- Must be investigated
- Must report those that occurred in your facility or in a facility that performed a manufacturing step for you under contract, agreement or other arrangement
- Only related to “core” CGTPs (1271.150(b))

# When, How, Where

- **As soon as possible, not to exceed 45 days after discovery**
- **www.fda.gov/cber/biodev/biodev.htm**
- **Form FDA-3486 and instructions**
- **Electronically or by mail**
- **HCT/P Deviation Codes**

# HCT/P Deviation Codes

| | |
|---|---|
| **DE** | Donor Eligibility |
| **DS** | Donor Screening |
| **DT** | Donor Testing |
| **EC** | Environmental control |
| **SR** | Supplies and reagents |
| **RE** | Recovery |
| **PC** | Processing |
| **LC** | Labeling control |
| **ST** | Storage |
| **SD** | Receipt, Pre-distribution Shipment, Distribution |

| HCT/P Deviation | FY '05 | FY '06 |
|---|---|---|
| Donor Eligibility | 8 | 22 |
| Donor Screening | | 10 |
| Donor Testing | | 19 |
| Environmental Control | | 1 |
| Supplies and Reagents | | 2 |
| Recovery | | 2 |
| Processing | | 11 |
| Labeling Control | 1 | |
| Storage | | 1 |
| Receipt, Pre-Dist., Distribution | 5 | 32 |
| Not reportable | 15 | 101 |
| **Total** | **29** | **201** |

# HCT/P Establishment Inspections

| Fiscal Year October-Sept. | # Inspections | # FDA-483s Issued |
|---|---|---|
| ’06 (to July 30) | 285 | 77 (27%) |
| ‘05 | 270 | 49 (18%) |
| ‘04 | 285 | 48 (17%) |
| ‘03 | 227 | 60 (26%) |
| ‘02 | 163 | 53 (33%) |
| ‘01 | 132 | 50 (39%) |

# HCT/P Inspections FY '06
# October 1, 2005 to July 30, 2006

| Type of Establishment | # Inspections | # FDA-483s Issued |
|---|---|---|
| Reproductive cells/tissues | 57 | 16 (27%) |
| Cord Blood and Peripheral Blood Stem Cell | 30 | 10 (30%) |
| All other (MS, Ocular) | 198 | 51 (28%) |
| **Total** | **285** | **77 (27%)** |

# Compliance Information www.fda.gov/cber/tissue/inspect.htm

- **Compliance Program 7341.002 (covers tissue recovered after 5/25/05)**
  - **July 1, 2005 through September 30, 2009**
- **Compliance Program 7341.002A (covers tissue recovered before 5/25/05)**
- **Note Attachments—box entitled "During the inspection,…"**

# Import Alert # 57-19 3/10/06

- **This guidance is for reviewing entries of Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/Ps) regulated solely under section 361 of the PHS Act and 21 CFR 1271.**
- **Note: HCT/Ps should be permitted to travel to the consignee under quarantine while FDA is determining admissibility, due to the perishable nature of most HCT/Ps.**

# Import Alert # 57-19 3/10/06

- Import Requirement Exceptions For Hematopoietic Stem Cells And Reproductive HCT/Ps FDA should act promptly to facilitate release of hematopoietic stems cells (derived from peripheral or cord blood) and reproductive HCT/Ps. The import requirements in 21 CFR 1271.420 do not apply to reproductive HCT/Ps donated by a sexually intimate partner of the recipient for reproductive use and generally do not apply to hematopoietic stem cells. FDA does not intend to review any entries of these HCT/Ps at the time of entry to verify compliance. Consequently, entry should be facilitated as promptly as possible. Should these products come up for review, permit them to travel to the consignee under quarantine.

# Top 10 FDA-483 Citations

- **Failure to [prepare] [validate] [follow] written procedures for prevention of [infectious disease contamination] [cross-contamination] during processing.**
- **Failure to [prepare] [follow] written procedures for all significant steps for [obtaining] [reviewing] [assessing] the relevant medical records of a donor.**
- **Procedures for all steps performed in the [testing] [screening] [determining] of donor eligibility of HCT/Ps were not [established] [maintained] [defined] [documented] [implemented] [followed] [reviewed] [revised].**

# Cont.

- **Procedures appropriate to meet core CGTP requirements for all steps that you perform in the manufacture of HCT/Ps were not [established] [maintained] [defined] [documented] [implemented] [followed] [reviewed] [revised].**
- **Failure to [prepare] [follow] written procedures for designating and identifying quarantined tissue.**
- **Human tissue intended for transplantation was not accompanied by a summary or copies of the donor's relevant medical records.**

# Cont.

- **Failure to maintain records which are [accurate] [indelible] [legible].**
- **Records fail to [identify the person performing the work] [include the dates of the various entries] [be as detailed as necessary to provide a complete history of the work performed and to relate the records to the particular tissue involved].**
- **Records fail to include documentation of receipt and/or distribution of human tissue.**
- **Records fail to include documentation of destruction or other disposition of human tissue.**

# Human Tissue Task Force

- **Multidisciplinary FDA task force (CBER and Office of Regulatory Affairs—ORA)**
- **Assess the effectiveness of the implementation of tissue rules-1 yr ago**
- **Are additional steps needed to assure tissue safety and availability?**
- **Review of recent findings at recovery establishments; take administrative and criminal actions**
- **Identify problems; propose changes to existing policies if necessary; identify resources needed**
- **Continue to work with professional organizations to support their ongoing efforts**

# Contact Information


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